EXHIBIT H

344TH STORY of Level 1 printed in FULL format.



McGraw-Hill's Biotechnology Newswatch

October 6, 1986

SECTION: Volume 6, Number 19; Pg. 8

LENGTH: 612 words

HEADLINE: DNA cleavage adapter groomed for genetic diagnostics

DATELINE: MADISON, WISC.

BODY:

By customizing DNA-cleaving enzymes, research scientists at the University of Wisconsin here have developed "an adapter that permits detection of a multiplicity of genetic disorders." So says its inventor, genetic engineer Dr. Waclaw Szybalski. He and co-worker Dr. Anna Podhajska, a microbial geneticist from the University of Gdansk, Poland, can alter the adapter to cut nucleic acid sequences at any site.

When applied to detecting point mutation on the human genome, Szybalski says, "the invention is easy to automate -- something hospitals could use. It doesn't require gels or blotting, just simple filtration." The adapter can be labeled radioactively, or not, "depending on the customer's preference."

Another new diagnostic tool, called by its inventor "DNA amplification," makes many copies of any sequence. Dr. Kary Mullis of Cetus Corp., Emeryville, Calif., explains that with his technique, "just a bit of DNA, all one often has from humans, can be increased in factors up to a million. Instead of looking for a needle in a haystack," he explains, "you cause whatever needle -- that is, sequence -- you're looking for to multiply. One can determine whether a fetus is homozygous for a trait by amplifying a crude cell lysate from amniocenteses." Dr. Mullis adds, "the technique could be used for AIDS virus detection, perhaps in blood bags. It allows us to look at a low number of viruses in a big number of cells"

"There is great potential for the use of Szybalski's cleavage technique in diagnostics," says Dr. Frances Barany, assistant professor of microbiology at Cornell University Medical College, New York City, "because you can tailor the enzyme to recognize any sequence you want, for example the particular mutation that makes a cell sickle."

Szybalski says his cleavage adapter "won't replace the existing 500 or so restriction enzymes that cut at 100 recognition sites . . . because they exist already. It's simplest to use the one in the refrigerator, less hassle, and cheaper to borrow or buy an enzyme for $60 to $100." An adapter costs about $70. Because one must synthesize a single DNA strand to lay over a strand of interest, he adds, the technique is "not notably easier [than standard methods requiring insertion of an engineered sequence], just longer or shorter; extra nucleotides cost more."

Szybalski's adapter looks like a DNA hairpin with one prong broken in half. The long prong is a variable single-stranded chain, synthesized to complement a given target sequence, over which it is laid. The hairpin's bend is a

Mullis 1/2/01
EXHIBIT
206

double-stranded constant site that wraps around and hooks onto one end of the target, creating a whole hairpin. A class IIs restriction enzyme, Fok 1, recognizes the constant site, and cuts nine or 13 nucloeotides down from it, within the unaltered target sequence. There are approximately fifteen Class IIs enzymes. All have the ability to recognize a site, and cut a specific distance away from it.

Mullis's technique uses oligonucleotides to "trim the sequence of interest out of whatever DNA it's in." Then the sequence duplicates itself in the presence of polymerase. Mullis notes, "You do get a lot of other things replicating that you don't want, but the background is low enough to be readable."

If Mullis's and Szybalski's inventions were combined, the result could be a "tremendously powerful diagnostic tool," Cornell's Barany suggests. "By combining the two techniques, you generalize the concept of using Cetus' polymerase chain reaction so that you can cut at any restriction site, which can be engineered for any sequence you want -- and do it in quantity."
URL: http://www.mhenergy.com/demos/biotech/index.html

LANGUAGE: ENGLISH